MODIFIED PTO/SB/33 (09-08)
Approved for use through 10/31/2008. OMB 0651-0031

PRE-APPEAL BRIEF REQUEST FOR REVIEW

		Docket Number Q94121
I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to "Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450" [37 CFR 1.8(a)] on _____	Application Number 10/574,477	Filed January 9, 2007
	Confirmation Number: 2361 First Named Inventor Masao SUDOH	
Signature Typed or printed name	Art Unit 1621	Examiner Sudhakar KATAKAM

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a Notice of Appeal.

The review is requested for the reason(s) stated on the attached sheet(s).
Note: No more than five (5) pages may be provided.

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I am the

☐ applicant/inventor.

☐ assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96)

☑ attorney or agent of record. Registration number 30,951

☐ attorney or agent acting under 37 CFR 1.34. Registration number if acting under 37 CFR 1.34 _____

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June 7, 2011
Date

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below*.

☑ *Total of 1 form is submitted.

PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of	Docket No: Q94121
Masao SUDOH, et al.	
Appln. No.: 10/574,477	Group Art Unit: 1621
Confirmation No.: 2361	Examiner: Sudhakar KATAKAM
Filed: January 9, 2007	

For: DRUG CONTAINING (2R)-2-PROPYLOCTANOIC ACID AS THE ACTIVE INGREDIENT

PRE-APPEAL BRIEF REQUEST FOR REVIEW

MAIL STOP AF - PATENTS
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Pursuant to the Pre-Appeal Brief Conference Pilot Program, and further to the Examiner's Final Office Action dated February 8, 2011, Applicant files this Pre-Appeal Brief Request for Review. This Request is also accompanied by the filing of a Notice of Appeal.

Applicant turns now to the rejections at issue:

Claims 1, 7, 8, 12-14, 16, 27, 28, and 33-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hasegawa et al (Bull. Chem. Soc. Jpn. 2000, 73, 423-428) or JP 8291106 in view of Ohuchida et al (US 6,201,021), Black (US 6,043,223), Toda et al (US 6,608,221) and Takada et al (US 2002/0022738 Al). Further, claims 1, 7, 8, 12-14, 16, 27, 28, and 33-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Honjo et al (EP 1 415 668 Al) in view of Nakaoka et al (JP 07285911 A) and Takada et al (US 2002/0022738 Al).

Applicants respectfully traverse the rejections for the reasons of record, which are incorporated herein by reference, and submit that (1) the cited reference does not disclose all elements of the present claims; and (2) the Examiner has failed to provide a reasonable technical basis for the assertion of inherency to meet missing elements of the claims as errors to be reviewed.

Claim 1 recites a liquid medicament for preparing injection, comprising a micelle water dispersion liquid of (a) (2R)-2-propyloctanoic acid or a salt thereof and (b) about 1 to about 5 equivalents of a basic metal ion based on 1 equivalent of (2R)-2-propyloctanoic acid or a salt thereof. The basic metal ion is supplied by at least one selected from a metal salt of phosphoric acid, and optionally a metal hydroxide. The medicament has a pH of about 8.4 to about 9.0.

None of the cited references disclose teach or suggest "a micelle water dispersion liquid" as presently claimed and therefore this element of the claims is not met. Instead the Examiner refers to Applicants' compound and states that Applicants' compound is expected to form a micelle water dispersion based on the concentration of components in the composition. This is improper since it is the Examiner's burden to establish that the prior art *necessarily* or inherently forms a micelle water dispersion. Thus, the Examiner's position is in error.

The Examiner's position is in error, since the Examiner cannot point to a single composition disclosed by any of the references which is similar to that of the present invention. First, one of ordinary skill would not combine or modify the references as suggested by the Examiner for the reasons already presented. Further, assuming *arguendo* that the cited references could be combined, as suggested by the Examiner, the claimed invention would not have been achieved. The Examiner's position is based primarily on improper hindsight reconstruction and the Examiner has not provided a reasonable technical basis for asserting that, even if the references could be combined, a micelle water dispersion liquid would be obtained.

The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993) (reversed rejection because inherency was based on what would result due to optimization of conditions, not what was necessarily present in the prior art); *In re Oelrich*, 666 F.2d 578, 581-82, 212 USPQ 323, 326 (CCPA 1981). "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.' " MPEP § 2112(IV). Therefore, it is improper for the Examiner to assert that several features of the claimed invention are optimizable such as the "possible salts", the amount

of the salt, and the amount of the basic metal ion in the composition, but that the claimed invention having distinct structural features and unexpected effects would be obtained if all factors were optimized to obtain it. **This is clear error**.

In relying upon the theory of inherency, the Examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art. In this case, the Examiner has not met this burden.

The Examiner relies on 6 different references, none of which teach the combination of the claimed (2R)-2-propyloctanoic acid or salt thereof and a basic metal ion supplied by at least one selected from a metal salt of phosphoric acid, a metal salt of carbonic acid and a metal salt of sulfuronic acid, much less having about 1 to 5 equivalents of a basic metal ion based on 1 equivalent of (2R)-2-propyloctanoic acid or salt thereof.

Further, the Examiner admits that Black teaches the use of sodium hydroxide to dissolve zaprinast and there is no teaching or suggestion of mixing (2R)-2-propyloctanoic acid with sodium phosphate. The Examiner also admits that Takada et al does not teach any similarity between its drug compound and (2R)-2-propyloctanoic acid or salt thereof. Additionally, Applicants have pointed out that more than 12,0000 times of the basic metal ion based on 1 equivalent of the active ingredient are included in the preparation of Black, whereas Applicants' claim a very narrow range of about 1 to about 5 equivalents of the basic metal ion based on 1 equivalent of (2R)-2-propyloctanoic acid or salt thereof. Neither of Hasegawa et al nor Hisao et al (JP '106) teaches or suggests a medicament comprising (2R)-2-propyloctanoic acid and a basic metal ion and Toda et al relates to a process which is not related to the claimed invention.

The references are completely silent as to the feature of a micelle water dispersion liquid of components (a) and (b). Yet, despite the facts that (1) there is no teaching, suggestion or mention of a micelle water dispersion liquid in any one of the six references; (2) there are several acknowledged differences between the claimed invention and the cited art; and (3) there is not one embodiment of a similar composition to that of the claimed invention in the cited references, the Examiner asserts that the "composition of the cited prior art" is expected to have micelle water dispersion of liquid of the compound.

The Examiner refers to Applicants' specification in support of his position in stating that the specification discloses that micelles, i.e., aggregates formed by (2R)-2-propyloctanoic acid or aggregates formed from the interaction of (2R)-2-propyloctanoic acid with a basic metal ion, are homogeneously dispersed in the medium and its properties are not significantly different from those of conventional aqueous solutions.

However, the specification refers to the property of "fluidity or the like" of the micelle water dispersion liquid. See page 23, lines 1-5. This disclosure in the specification means that although the micelle water dispersion liquid contains aggregates, it maintains fluidity properties similar to those of conventional aqueous solutions and, therefore, is still useful as a liquid medicament for preparing injections as claimed. Such a micelle water dispersion liquid for preparing injections which shows fluidity properties similar to those of conventional aqueous solutions are not described or indicated in the prior art. Nor does the prior art recognize the advantages of such a feature, which allows for high concentrations of (2R)-2-propyloctanoic acid while maintaining operability equal to that of aqueous solutions. See page 23 of the specification, lines 6-11. For at least this reason, the present invention is not rendered obvious by the cited references, whether taken alone or in combination.

The Examiner appears to misunderstand this structurally distinguishing feature of the claimed invention and the Examiner did not specifically address this point in the Final Office Action.

Applicants further submit that Honjo does not disclose a basic metal ion as part of the composition, much less the amount of basic metal ion. Further, Honjo is silent as to the feature of a micelle water dispersion liquid and it can not be said that this feature is inherent in the composition of Honjo. There is no teaching or suggestion of this feature and the compositions do not contain the same components in the same amount as claimed. Thus, the Examiner has not met his burden of establishing that the composition of Honjo *necessarily* meets the element of a micelle water dispersion liquid.

Neither of Nakaoka nor Takada remedy this deficiency since these references also fail to disclose, teach or suggest a similar composition having the same components and same amount or the feature of a micelle water liquid dispersion. Additionally, one of ordinary skill in the art would not have been motivated to combine the references as suggested by the Examiner,

Nakaoka is directed to compositions having improved heat-resistance and useful as a raw material for metallic soap and for various esters. One of ordinary skill in the art would not have been motivated to therefore combine Honjo directed to a pharmaceutical composition for the treatment of cerebral ischemic diseases and Nakaoka which is directed to forming a raw material for metallic soap and various esters with a reasonable expectation of success in achieving the claimed invention. Further, Takada do not teach or suggest any similarity between the drug compound of Takada et al and (2R)-2- propyloctanoic acid or salt thereof. Thus, one of ordinary skill in the art would not have been motivated to combine the references as suggested by the Examiner. Even if the references were combined the claimed invention would not have been achieved.

Moreover, the present invention provides unexpectedly superior results over the prior art. As shown by the Declaration submitted November 29, 2010, the present invention has the following remarkable effects that: (1) (2R)-2-propyloctanoic acid, which is insoluble in water, can be dissolved in water in high concentrations in the medicament of the present invention; (2) the medicament of the present invention has resistance to pH fluctuations using solution and/or dilution liquid before use; and (3) it is possible to prepare an infusion which has a pH that can be administered to patients without clouding. Such remarkable effects could not have been expected based on the cited references. For this additional reason, the present invention is patentable over the cited references.

Accordingly, Appellants respectfully request the Pre-Appeal Brief Conference Panel to withdraw the foregoing rejections in view of clear error.

Respectfully submitted,

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